

June 1883

SARCOMA OF THE BLADDER.

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REPRINTED FROM THE "MEDICAL CHRONICLE," JUNE AND JULY, 1883.



JOHN HEYWOOD,
DEANSGATE AND RIDGEFIELD, MANCHESTER;
AND 11, PATERNOSTER BUILDINGS,
LONDON.
1888.

SARCOMA OF THE BLADDER.

IT is generally stated that sarcomatous tumours of the bladder are of rare occurrence in comparison with the other varieties of neoplasm met with in this situation. According to Stein,¹ "Sarcoma is one of the rarest diseases of the bladder, there are but few authentic cases on record."

Reginald Harrison² says : "Sarcoma of the bladder is a very rare growth." Sir Henry Thompson, in his work on *Tumours of the Bladder* (1884), writes : "The existence of true sarcoma of the bladder has been affirmed, but not on the observation of fresh specimens." He describes, however, a class of tumours which "appears to be best indicated by using the term 'transitional' to describe it, as, perhaps, occupying a place between papilloma and a formation of malignant type—sarcoma." A characteristic feature is the presence in the ground substance of groups of variously-shaped cells, generally arranged in definite groups, which do not belong to normal tissue on the one hand, or to distinct new growth on the other. He suggests that the presence of these cells has, perhaps, led some observers to pronounce such structures to be sarcoma, and adds, "before long it is not improbable that some unquestionable example will be met with and identified."

It is interesting to note that in an account of six cases of tumour of the bladder recently removed by Sir Henry Thompson,³ two are described as of this nature, one being a round-celled, the other a chondrifying sarcoma ; the remaining four were papillomata. From an examination of eighteen cases of primary tumour of the bladder which have been under the care of my colleagues or myself during the last two years,⁴ it would appear that this form of growth is of much more common occurrence than is generally believed. No less than six—*i.e.*, one-third of the number, being examples of sarcoma. It is, therefore, very probable, as both

¹ "A Study of the Tumours of the Bladder," 1881, p. 33.

² "Surgical Disorders of the Urinary Organs," 1887, p. 552.

³ *Clinical Society Transactions*, 1887, p. 63.

⁴ Two of the patients were under my care ; the others were under my colleagues, Dr. Simpson, and Messrs. Heath, Whitehead, and Jones, who kindly allowed me to examine and take notes of the cases. (Of the remaining twelve cases, eight were examples of papilloma, four of carcinoma.)

Stein and Gross have suggested, that many cases formerly described as encephaloid cancer were in reality of this nature, for without a careful microscopical examination it is often impossible to distinguish between them.

The following observations are based upon a consideration of the six cases just referred to, and twenty-eight cases of sarcoma, which have been recorded by various writers.

Primary or Secondary.—Sarcoma usually involves the bladder primarily, as in all the six cases referred to, and as in most of the recorded cases. Much less frequently the bladder is secondarily affected, as the result of direct extension from some adjacent part, *e.g.*, the prostate in males, or the walls of the vagina in females; the latter condition was met with in three cases quoted by Stein,⁵ and also in another reported by Howard Marsh.⁶ In two recorded instances the bladder was involved secondarily in consequence of generalisation of a sarcomatous tumour, originating in some distant part, *e.g.*, in the cranium,⁷ and in the eyeball.⁸

Etiology.—As in the case of other forms of vesical tumour, the etiology of primary sarcoma of the bladder is usually very obscure. In a few recorded instances the growth appears to have been directly due to local irritation, the patient having previously passed gravel or small calculi.⁹ Other causes of long-continued irritation, *e.g.*, stricture of the urethra, chronic urethritis, enlargement of the prostate, &c., may also act in the same way, and this view is supported by the fact that, like other neoplasms in this situation, sarcoma of the bladder is much more common in males than females (*vide infra*), the urinary and genital disorders of the former sex doubtless playing an important part in its production. (In one of the six cases the patient had previously been treated for a stricture of the urethra, and was suffering from a urinary fistula of long duration.) It is not improbable that simple growths, *e.g.*, papillomata, may, after a time, change their character, and take on sarcomatous action, for in several specimens of papilloma recently examined by my friend Dr. Railton and myself, the deeper parts of the tumour have been

⁵ *Op. cit.*, p. 85.

⁶ *Path. Soc. Trans.*, Vol. 25, p. 178.

⁷ *Path. Soc. Trans.*, Vol. 34, p. 212.

⁸ Thompson. "Tumours of the Bladder," p. 63.

⁹ R. Williams.—*Lancet*, 1882; *Univ. Coll. Hosp. Reports*, 1884, p. 43.

found infiltrated with groups of cells of a very suspicious nature, and the connective-tissue stroma has not been so perfectly formed as one would expect in a growth of a purely simple kind. This is especially likely to be the case when recurrence takes place after removal, as in an instance recently under my care: the primary tumour was a typical papilloma, while the recurrent growth was in places distinctly sarcomatous.

Age.—The ages of the patients in the six cases were as follows:—9, 40, 46, 47, 60, 69 years. If these are included with the 28 recorded cases, the ages may be arranged as follows:—

Under 10 years	10 cases.
10—20 years	0 "
20—30 years	3 "
30—40 years	1 "
40—50 years	4 "
50—60 years	8 "
60—70 years	7 "
70—80 years	1 "

34

It would appear, therefore, that sarcoma is most common at two periods of life, viz., under ten, and between forty and seventy years of age. It is the form of growth most commonly met with in young subjects, and it is not improbable that many of the recorded cases of myxoma and fibroma of the bladder (so-called mucous and fibrous polypi) in children, were really of this nature. In its relatively frequent occurrence at an early period of life, sarcoma of the bladder may be compared with sarcoma of the testis, which, as Butlin¹⁰ has pointed out, is most common in persons under ten years of age, and between thirty and forty, a large proportion of cases being also met with in persons over fifty years of age (in 41 cases of sarcoma of the testis the subjects were in nine instances not more than ten years old).

Sex.—Of the six cases, five occurred in males, one in a female; of the entire thirty-four cases, twenty-four occurred in males, ten in females. Like other forms of tumour of the bladder, sarcoma is, therefore, much more common in the male than in the female sex.

Origin.—When attacking primarily the wall of the bladder, sarcoma usually originates in the connective tissue of the submucous layer; as

¹⁰ "Sarcoma and Carcinoma," p. 22.

the growth progresses, its tendency is to invade the muscular coat, and, in some instances, even extend beyond it, and involve the surrounding tissues (*vide infra*). In three of the six cases where the bladder was examined after death, infiltration of the muscular coat was found to be present.

Situation.—In four instances the growth was connected with the base, or base and posterior wall, of the bladder. In one instance it was very diffus, involving, in addition, the whole of the right lateral wall. In another, it sprang from the anterior wall on a level with the upper border of the pubes. From a consideration of the thirty-four cases, it appears that though sarcoma, like other forms of tumour, most commonly involves the base and posterior wall, yet it is not very uncommon to find it affecting the anterior and lateral walls as well as the summit itself. In rare instances, almost the whole of the inner surface of the bladder has been found invaded by the growth.¹¹

Form, Size, and Number.—In most cases one or more distinct tumours are present projecting into the interior of the bladder, as in five of the six cases. The tumours are usually sessile, with a broad base of attachment (four cases), less frequently distinctly pedunculated (one case). In the sixth case there was not a distinct tumour, but a diffuse growth involving a large extent of surface. When several tumours are present they are often clustered together so as to form a single mass, which may attain considerable dimensions, in one case almost entirely filling the cavity of the bladder. When occurring in young subjects, sarcoma usually appears in the form of multiple polypoid growths, varying in size from a pea to a walnut, or sometimes larger.

Consistence and Surface.—The growth may be firm throughout, and irregularly lobulated or fissured, presenting a cauliflower-like appearance; or the surface may be soft and villous, the deeper part being of denser consistence. In other cases the entire growth is soft and fluffy resembling very closely a papilloma.

*Minute Structure*¹².—In three of the cases the tumour was a round-celled sarcoma; in one of these the cells in places were contained in alveoli, presenting the appearance usually described as “alveolar

¹¹ R. Williams, *Brit. Med. Journal*, 1882. II. p. 78.

¹² I am indebted to my friends, Drs. Railton and Larmuth, for sections of the different tumours.

sarcoma"; in another, portions of the growth were composed of a delicate fibrillated network, in the meshes of which the cells were enclosed, presenting all the characteristics of a lympho-sarcoma. In the remaining three cases the tumour was a mixed-celled sarcoma, being, made up of round and spindle cells in varying proportions.

In three of the cases (two mixed-celled, one round-celled) the surface of the tumour was distinctly villous. The villi, some of which were long and slender, others short and thick, were invested with one or more layers of elongated columnar or oval cells, set at right angles to the long axis of the villus. In addition to capillary vessels, the stroma of the villi contained numerous cells, either round or spindle-shaped, similar to those which made up the bulk of the growth. Though it appears that sarcoma of the bladder usually occurs as a round or mixed celled growth, yet other varieties have been met with. Spindle-celled tumours have been described by Senftleben¹³ and Chiari.¹⁴ R. Williams¹⁵ has found giant cells intermingled with round and spindle cells. Langton¹⁶ records a case of alveolar sarcoma; Eve¹⁷, Chaffey¹⁸, and Williams¹⁵ cases of lympho-sarcoma. Sir H. Thompson refers to a case of melanotic sarcoma¹⁹ (secondary to a growth in the eyeball), and describes one of chondro-sarcoma²⁰.

Local Extension.—The growth usually remains confined to the walls of the bladder, as in three of the six cases, where the part was examined after death, and in five cases described by Williams¹⁵. Less frequently it spreads beyond it, infiltrating adjacent parts by direct extension, as in a case recorded by Morrant Baker²¹, where the rectum had become fixed and surrounded, a fistulous opening having formed between it and the bladder. In Chiari's¹⁴ case, the growth had invaded the prostate and vesiculae seminales.

Secondary Deposits.—Secondary deposits in other parts of the body are much more frequently absent than present, for in three of the six cases where an opportunity was afforded of examining the body after

¹³ *Arch. für klin. Chir.* 1860.

¹⁴ *Prager med. Wochenschrift*, 1886. No. 50.

¹⁵ *Brit. Med. Journal*, 1882. II., p. 78.

¹⁶ *Lancet*, 1885. II., p. 1185.

¹⁷ *Path. Soc. Trans.*, 1885, p. 284.

¹⁸ *Path. Soc. Trans.*, 1885, p. 288.

¹⁹ "Tumours of the Bladder," p. 63.

²⁰ *Op. cit.*, also *Path. Soc. Trans.*, 1887, p. 183.

²¹ *Lancet*, 1886. I., p. 737.

death they were only met with once, viz., in one kidney²². In two recorded cases²³ secondary deposits were found in the lungs, and in another instance, in both lungs and liver²⁴. The lymphatic glands always escape infection.

Condition of Bladder.—In consequence of the obstruction to the escape of urine, or from the long-continued irritation produced by the presence of the growth, evidences of chronic cystitis are sooner or later produced: in some cases, the bladder is small and contracted with hypertrophy of its walls, while in others the opposite condition of dilatation is found to be present. In one of the six cases ulceration and perforation of the bladder-wall had taken place, and an abscess, which had formed externally, had opened into the abdominal cavity, setting up peritonitis, which was the cause of death. In another, the anterior wall of the bladder had given way in consequence of retention of urine, and hyper-distension of the viscus with blood-clot.

Secondary Changes in Kidneys.—As in other forms of bladder-tumour, secondary changes of a degenerative kind are after a time usually produced in the kidneys; either dilatation of the pelvis and calices, with absorption of the secreting structure of the gland, owing to the obstruction offered by the tumour to the entrance of the urine into, or its escape from, the bladder (this condition was present in all three cases where the kidneys were examined after death); or suppurative pyelitis or nephritis, in consequence of extension of inflammation from the bladder when cystitis is present. In rare cases, as already mentioned, the kidneys may also become affected with secondary deposits.

Symptoms.—The general symptoms of sarcoma of the bladder are very similar to those met with in other varieties of vesical growths, consisting of haematuria with signs of irritability of the bladder, viz., pain and increased frequency in micturition; in most cases evidences of obstruction to the escape of urine are sooner or later produced, micturition becoming difficult and attended by straining efforts. In addition, attacks of retention and incontinence of urine are sometimes present in the later stages, and in some instances distinct evidences of the existence of the growth can be detected upon a physical examination of the bladder.

²² In the case (already referred to) of papilloma recurring after removal, where the recurrent tumour had in places taken on sarcomatous action, a secondary deposit was found in the sacrum.

²³ Marchand.—*Archiv. für Klin. Chir.*, 1878. *Univ. Coll. Hos. Reports*, 1884, p. 43.

²⁴ Baker.—*Op. cit.*

Hæmaturia is usually a prominent and often an early symptom. It frequently precedes the signs of irritability of the bladder, so that in this respect sarcoma resembles papilloma—for, as Sir H. Thompson has pointed out, a painless haemorrhage often continuing for a considerable period, sometimes for several years, without any other symptoms, is generally characteristic of the latter affection. As in papilloma, the bleeding at first occurs in attacks separated by intervals of varying duration, during which the urine is quite clear. As the disease progresses, the attacks last longer and become more frequent, until after a time the urine is never free from blood. This was the history in four of the six cases, hæmaturia having been present for periods respectively of 5 years, 18, 12, and 3 months, before evidences of irritation of the bladder were observed.

In other instances, blood may appear in the urine, and at the same time micturition becomes painful and increased in frequency, as in one case where these symptoms appeared simultaneously and had been present for a period of two years when the patient came under notice.

In other cases, again, hæmaturia may be a late symptom, for in one instance it only appeared a week before death, being preceded for a period of three months by evidences of irritability of the bladder. When this happens, sarcoma resembles cancer of the bladder, for in the latter affection (contrary to what is the rule in cases of papilloma) pain and frequency in micturition usually precede the appearance of blood in the urine.

Occasionally hæmaturia is absent throughout the entire course of the case, as in one instance recorded by Marchand,²⁵ where for two years the only symptoms were those of vesical catarrh; and in another described by Chaffey,²⁶ where for more than twelve months the patient suffered from difficult and painful micturition, no blood being ever observed in the urine.

When hæmaturia is present, the quantity of blood varies; in some cases it is very considerable, large clots being passed in addition to almost pure blood; in other cases it may be very slight, merely staining the urine. As in other cases of vesical haemorrhage, the blood is usually present in greatest quantity towards the end of micturition, and bleeding

²⁵ *Arch. für klin. Chir.*, 1878, XXII. p. 676.

²⁶ *Path. Soc. Trans.*, Vol. XXXVI., p. 287.

is generally excited or increased after the introduction of instruments into the interior of the bladder. In one instance, where the symptoms at first pointed to caleulus, it was the onset of somewhat profuse and continuous hæmaturia after sounding the bladder, and the absence of any evidence of the presence of a stone, that excited suspicion as to the existenee of a growth.

Pain and Frequent Micturition.—As already stated, micturition, sooner or later, beeomes painful and increased in frequency ; for the tumour, as it increases in size, projects into the interior of the bladder and irritates the mucous membrane, whieh consequently becomes affected with chronic inflammation. In some cases pain is slight and only complained of during micturition ; in others, and especially in the later stages, it is very severe and almost constantly present ; it may be felt only in the perineum and at the neck of the bladder, or in the thighs, buttocks, and lower part of the abdomen ; or (as in two cases) it may be referred chiefly to the end of the penis.

Difficult Micturition.—After a time, micturition usually becomes more or less diffieult and accompanied by straining efforts. This is especially likely to occur when the growth involves the neck of the bladder, or when (as in one case) it possesses a pedicle, so that it can fall against and obstruct the vesical orifice of the urethra.

Sudden Stoppage in Stream.—Under the same circumstances (in two cases) there may be oecasional sudden stoppages in the stream of urine, which is only restored after severe straining ; this symptom is also sometimes observed independently of these causes, if large elots of blood passed with the urine become temporarily arrested in the urethra.

Retention of Urine.—Occasionally the obstruction produced from one or other, or a eombination of the preceding causes, is so complete that retention of urine results. This condition was present in one instance, the vesical orifice of the urethra being blocked by the growth and the bladder being also filled with a firm blood-clot.

Incontinence of Urine.—Incontinence of urine may be present under these circumstances (as happened in the case just referred to) as the result of overflow from the distended bladder, evidences of which can usually be detected. In other instances the urine may continually dribble away independently of distension, probably as the result of simple “gagging” or dilatation of the vesical orifice of the urethra by

the growth when situated at the neck of the bladder, for in two of the cases incontinence was a prominent symptom without any signs of distension being present.

Condition of the Urine.—Except for the presence of blood, the urine may for a considerable period retain its normal character. As soon, however, as cystitis is set up, it presents the changes which are usually associated with that condition, becoming alkaline in reaction and depositing a quantity of ropy, viscid mucus. Examined microscopically, it will be found to contain, in addition to blood, pus and epithelial cells, often in considerable quantity, along with crystals of triple phosphate, &c. The latter condition was present in three of the six cases; in five cases the urine was of low specific gravity (1009—1015), indicating, as was proved in three cases where an autopsy was made, the co-existence of secondary renal disease.

As in other cases of vesical tumour, the condition known as "fibrinuria" may occasionally be observed, for Weir²⁷ describes an instance where the urine was found to become "almost jellied from effused fibrin." It is only very exceptionally that distinct portions of growth are met with in the urine. In this respect sarcoma resembles cancer and differs from papilloma, for in the latter affection shreds of tissue, which examined microscopically are found to consist of typical villi, can frequently be detected in the urine. This is doubtless to be accounted for by the denser and firmer nature of the tumour in most cases of sarcoma, and also by the fact that even when the surface of the tumour is villous, the villi are not so long and slender as in papilloma, and are therefore less likely to be detached and come away with the urine. In none of the six cases were particles of growth detected in the urine.

Lange,²⁸ however, describes a case where "small, fleshy lumps of tissue" sometimes the size of a small cherry, were discharged with the urine. Under the microscope they showed the presence of large nucleated cells, similar to those found after removal in the tumour itself, which was a round-celled sarcoma.

Physical Signs.—When the tumour is of firm consistence, and of considerable size, its presence can sometimes be detected on digital

²⁷ *Medical News*, 1886, II., p. 623.

²⁸ *Medical News*, 1886, II., p. 639.

examination *per rectum* or *per vaginam*, or upon bimanual palpation, or upon exploring the bladder with a sound, as in many cases of cancer. Under these circumstances, it will, however, be felt, not as a hard irregular induration, a condition which is usually characteristic of cancer, but rather as an indistinct fulness, or a smooth, elastic swelling. In two of the six cases the presence of the growth was distinctly recognised by these means.

When, on the other hand, the tumour is of softish consistency, it will often escape detection on examination by any of these methods, as in papilloma; this was the case in three of the six patients. It is not improbable that under these circumstances, and especially when its surface is villous, washing out the bladder with a current of water might detach and bring away particles of growth of sufficient size to enable the existence of the tumour and its nature to be recognised, and also that the same might happen if a portion of it became caught in the eye of the catheter, as is frequently the case in papilloma.

In females, as the result of the constant straining during micturition, the growth, becoming protruded by the expulsive efforts of the bladder, may project from the urethra so that it is visible externally. This condition was met with in the case of a woman, aged 29 years, recorded by Senftleben,²⁹ a reddish, fleshy mass appearing at the meatus during straining at stool; and also, in another case, a female child, aged two years, described by Howard Marsh,³⁰ a fleshy-looking substance almost as large as a grape, protruding from the vulva.

It is only in the advanced stage of the disease, as already mentioned, that infiltration of the parts external to the bladder, the result of the direct extension of the growth, can be detected during life.

The recent improvements in the construction of the cystoscope render it probable that electric illumination and examination of the interior of the bladder by means of this instrument, will prove of assistance in detecting the presence of sarcoma, just as in the case of other forms of vesical tumour.³¹

Diagnosis.—The diagnosis of sarcoma from the other varieties of

²⁹ *Arch. für klin. Chir.*, 1860.

³⁰ *Path. Soc. Trans.*, Vol. XXV., p. 178.

³¹ For a full description of the Electric or Incandescent-lamp Cystoscope, and the method of using it, see "The Electric Illumination of the Bladder and Urethra." By E. Hurry Fenwick. London: Churchill. 1888.

tumour most commonly met with in the bladder, viz., papilloma and cancer, is often difficult, and in many cases quite impossible. When the growth is of such soft consistence that its presence cannot be detected on examining the bladder in any of the ways already mentioned, and when recurrent attacks of haematuria have been the early symptoms, then it is almost impossible to distinguish the case from one of papilloma. When, on the other hand, the tumour is dense and firm, so that it can be distinctly felt, the case may closely resemble one of cancer, and especially if signs of irritability of the bladder have preceded the appearance of blood in the urine. Under these circumstances, however, as already pointed out, the swelling is not so irregular, and the induration is not so marked as in the latter affection. The age of the patient may in some cases be of assistance in diagnosis, for while sarcoma is relatively somewhat common in young subjects, papilloma ³² is almost unknown before puberty, and cancer is rarely met with under forty years of age.

Course and Duration.—Sarcoma of the bladder, if allowed to run its course, sooner or later terminates fatally, usually within a period of from one to three or four years, death being due either to exhaustion from loss of blood and the pain and suffering from interference with micturition, or to some secondary renal or other complication, as in other forms of vesical tumour.

In one case, where no operative interference was adopted, symptoms had only been present for about three months, but here the immediate cause of death was ulceration and perforation of the bladder-wall, followed by the formation of a pelvic abscess which burst into the peritoneal cavity; in another, where the fatal result was again due to a very unusual complication, viz., rupture of the bladder from over-distension with urine and blood-clot, the history of the case only lasted over a period of eighteen months.

Treatment.—Inasmuch as palliative treatment is of little use, the bladder should be explored and an attempt made to remove the growth in the usual way, viz., with Thompson's forceps, by scraping with a Volkmann's spoon or the finger nail, or by means of some form of *écraseur*.

In some instances, as for example, when the growth is easily within

³² In 92 recorded cases of papilloma, the youngest patient was 18 years of age, this being the only case met with under 20 years.

reach of the finger, and of moderate dimensions, or pedunculated, this can be effected through a perineal opening in males, or through the dilated urethra in females. In one case (male) the tumour was removed twice from the perineum, and in another (female) *per urethram*, without much difficulty.

In all cases, however, and especially when the growths are multiple, sessile, and of large size, or if the perineum is deep and the patient stout, more complete access will be obtained through a supra-pubic opening. In one instance the growth was removed by supra-pubic cystotomy, after exploring the bladder from the perineum, its diffuse nature rendering its extirpation by the latter route impracticable.

If on exploring the bladder, either from the perineum or from above the pubes, the growth, from its nature and connections,—*e.g.*, if it is sessile and of firm consistence, extensively infiltrating the bladder-wall—is found to be not easily removable, or if its removal would be attended by danger, then it is a question whether it is not advisable to leave it, simply providing free bladder-drainage by establishing a urinary fistula on the same principle as in cases of cancer, namely, with the object of providing an outlet for the escape of urine, and in this way of relieving the pain and straining efforts which attend the frequent and ineffectual attempts at micturition. At the same time, by maintaining the bladder in a state of physiological rest, haemorrhage will be checked or diminished; while by frequently washing out the viscera with some antiseptic lotion, the inflammation of its walls can be relieved, and the offensive character of the urine, which when present, is in itself a source of irritation, can also be corrected. In one case, where on opening the viscera from above the pubes, a firm sessile growth was found involving its base and neck, no attempt was made at removal, the bladder being simply drained through the supra-pubic wound.

Recurrence after Removal.—As regards the question of recurrence after removal, this is to be expected, especially when the growth is sessile and infiltrates the wall of the bladder, so that its complete extirpation is almost practically impossible. In one case, where, these conditions were present, evidences of a return of the growth were found at an interval of three months after operation, and it was again removed, death taking place about four months subsequently to the second operation. In another case, however, where a very diffuse growth was removed, nearly

a year has now elapsed and the patient is still in the enjoyment of good health and free from any bladder symptoms.

In a case recorded by Morrant Baker,³³ the tumour quickly recurred and death took place about four months after operation, while in another, described by Weir,³⁴ evidences of a return were observed after an interval of six months. Sir H. Thompson³⁵ mentions a case where the growth reappeared in the course of three months, and another where removal was not followed by much benefit, death taking place about nine months after operation, the bladder containing a large recurrent tumour.

When, however, the tumour is pedunculated and therefore capable of being more completely removed, the prognosis is, of course, much more favourable, but further information on this point is required before anything definite can be said as to the chance of a permanent cure. In one case where this condition was present, the patient is free from any evidence of a return of the growth at an interval of nine months after operation.

Results of Operative Interference.—From a consideration of these results, it would appear that recurrence is very likely to take place after operation, and even if not locally, possibly in some other part of the body; still, life is undoubtedly prolonged, and symptoms are relieved by a removal of the tumour, though this may not be complete. In cases where the tumour is found to be not removable on opening the bladder, the free drainage which the operation will secure will always afford relief, so that under these circumstances, even supposing that life is not prolonged, benefit will always be derived from operative interference.

³³ *Lancet*, 1886, II., p. 737.

³⁴ *Medical News*, 1886, II., p. 624.

³⁵ *Clin. Soc. Trans.*, 1887, p. 64. *Path. Soc. Trans.*, 1887, p. 185.

